UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/975,519	11/20/97	ZHANG C	INGN.028

HM12/0624

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EXAMINER	
MOSHER,M	
ART UNIT	**PAPER NUMBER**
1643	11

DATE MAILED: 06/24/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/975,519	Zhang et al
Examiner	**Group Art Unit**
Mosher	1643

☒ Responsive to communication(s) filed on *10/7/98, 1/11/99*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *2-15, 20-30, 53-56, and 70-120* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *2-15, 20-30, 53-56, and 70-120* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *8, 10*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 USC § 112

Claims 2-15, 20-30, 53-56, 70-100, 106, 109, 119, and 120 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

New claims 119 and 120 recite "wherein the perfusion is achieved by a fed-batch process" and "wherein the perfusion is achieved by continuous perfusion". The ordinary meaning of the term "perfusion" necessarily implies a continuous process which is distinct from a fed-batch process, see for example the textbook by Cartwright, particularly the passages marked on pages 60-62. In the first Office action, this term was interpreted according to its usual meaning in the fermentation art. However, applicant is allowed to be his own lexicographer, and it appears that the intent is for "perfusion" to mean something other than its normal meaning of a continuous process. If the term "perfusion" is meant to encompass fed-batch processes, then it is not clear what applicant means by the term "perfusion", and all of the claims which involve "perfusion" are now rejected as indefinite. This new rejection of claims 2-15, 20, 22-30, and 53-56 was necessitated by the addition of claims 119 and 120.

Claim 21 is indefinite, as it depends from canceled claim 1. For purposes of examination, this claim will be treated as if it depended from claim 20. However, this treatment does not relieve applicant of the burden of response to this rejection.

In addition, in claims 22, 92, and 108, it is not clear what is meant by "the chromatography step comprises essentially a single chromatography step", because "comprises" is open in scope but "essentially a single step" is not open. It is also not clear what is the difference between "a single chromatography step" and "essentially a single chromatography step", since it is not clear how one could add more than one chromatography step without changing the essential nature of a single step. While the use of "consisting essentially of" a compound has a recognized meaning in defining ingredients in a composition, the meaning of "comprising essentially a single chromatography step" in defining a method is not clear. This affects dependent claims 23-27, 93-97, and 109.

Claim 56 lacks antecedent for "said adaptation".

Claim 71 is confusing in reciting "less between". Is the intent less than 0.7 or between 0.7-1.7?

Claims 2-15, 20-30, 53-56, and 101-120 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 20, 101, 110, and 118 now recite "a method for producing a pharmaceutically acceptable adenovirus composition". Specification page 72 indicates that "pharmaceutically acceptable" involves a composition "essentially free of pyrogens, as well as any other impurities that could be harmful to humans or animals". Since the specification provides no data on pyrogen content of the purified virus compositions, or on the

absence of potentially harmful impurities, one skilled in the art would have reason to doubt the assertion that virus compositions, purified according to the method steps recited in the claim, are necessarily pyrogen-free and lacking in potentially harmful impurities. Considering the well-known difficulties of preparing pyrogen-free compositions from biological materials, and considering the limited guidance and lack of working examples of compositions meeting the standards set forth in the specification for "pharmaceutically acceptable compositions", it is concluded that undue experimentation would be required to enable the pharmaceutically acceptable compositions, as now claimed.

Claims 101, 106-109, 118-120 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. New claims 101 and 118 recite "using a lysate technique other than freeze-thaw". While specification pages 29-36 discuss a variety of methods of lysing cells, including freeze-thaw, the specification does not reasonably support specific exclusion of the freeze-thaw method. Although Table 1 on page 30 does identify this method as "not scalable, not recommended for large scale manufacturing", the table also identifies other methods as "scalability concerns". Although the specification reasonablely conveys a variety of methods for lysing cells, the specification is not seen as reasonably conveying the concept of "any method except freeze-thaw", which is now the scope of the subject matter of these claims. This affects dependent claims 106-109 and 119-120.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 110-113, 115, and 116 are rejected under 35 U.S.C. 102(b) as being anticipated by Huyge et al (C14). Huyge et al teaches a method for preparing an adenovirus composition, using DEAE chromatography. The reference teaches that the DEAE-purified composition contains a small amount of host cell contamination, see for example page 1411, last paragraph. While the host cell material could be removed by further chromatographic steps, there is no indication that the small amount of host cell material contained pyrogens or materials harmful to animals and humans. Therefore, although the product of a single chromatography step is not the most pure composition taught by the reference, there is nothing on this record that distinguishes the product of the single chromatographic step from a "pharmaceutically acceptable composition" as claimed.

Claims 101-104, 108, 110, and 115 are rejected under 35 U.S.C. 102(e) as being anticipated by Munford et al, US 5,744,304. See column 17, lines 19-38.

Information Disclosure Statement

In the Information Disclosure Statement filed October 7, 1998, the International Search Report for PCT/US97/21504 has not been considered, because the copy provided was incomplete, missing form PCT/210 second sheet, first page (page 1 of 2, listing classification and documents considered to be relevant).

In the Information Disclosure Statement filed January 11, 1998, the PTO-1449 does not include a publication date for the provisional application 60/026,667. Since this application formed the basis for WO98/00524, it is presumed that the date of public availability for the provisional application is the same as the 1/8/98 publication date of the WO patent, and that the provisional application therefore does not qualify as a prior publication.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chris Eisenschenk, can be reached on (703) 308-0452. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196 .

June 21, 1999

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600